(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
5 January 2006 (05.01.2006)

PCT

(10) International Publication Number
WO 2006/002240 A2

(51) International Patent Classification:
G06F 15/16 (2006.01)

(21) International Application Number:
PCT/US2005/022071

(22) International Filing Date: 20 June 2005 (20.06.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/581,312	19 June 2004 (19.06.2004)	US
60/581,977	21 June 2004 (21.06.2004)	US
60/643,475	12 January 2005 (12.01.2005)	US
60/663,722	22 March 2005 (22.03.2005)	US

(71) Applicant *(for all designated States except US)*: **CHONDROGENE, INC.** [CA/CA]; 800 Petrolia Road, Unit 15, Toronto, Ontario M3J 3K4 (CA).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **LIEW, Choong-Chin** [CA/CA]; 81 Millersgrove Drive, Toronto, Ontario M2R 3S1 (CA). **YAGER, Tom** [US/CA]; 1268 Cermel Drive, Mississauga, Ontario L5H 3V4 (CA). **DEMPSEY, Adam** [CA/CA]; 26 Olive Avenue, Suite LPH07, Toronto, Ontario M2N 7G7 (CA). **CHAO, Samuel** [CA/CA]; 114 Glen Shields Avenue, Concord, Ontario L4K 1T6 (CA).

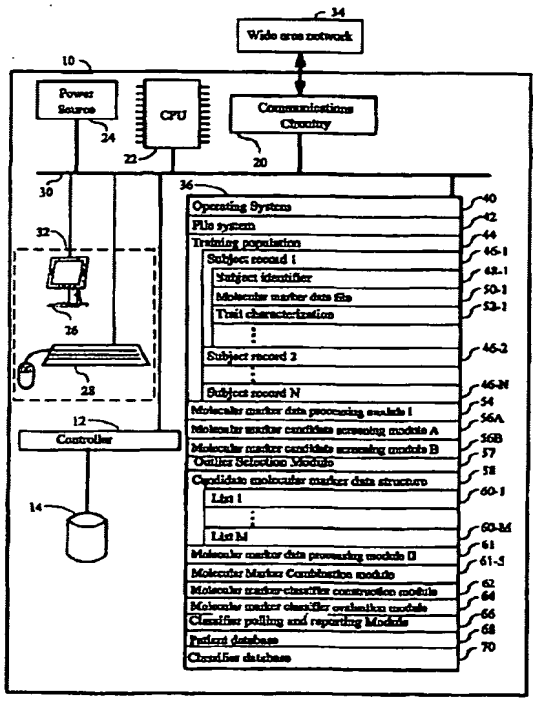
(74) Agents: **CORUZZI, Laura, A.** et al; Jones Day, 222 East 41st Street, New York, NY 10017-6702 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH,

[Continued on next page]

(54) Title: COMPUTER SYSTEMS AND METHODS FOR CONSTRUCTING BIOLOGICAL CLASSIFIERS AND USES THEREOF



(57) Abstract: The present invention provides systems and method for constructing classifiers that distinguish between trait subgroups using molecular marker data from blood samples. The invention further encompasses the use of the classifiers and combinations of molecular markers identified by the classifiers in a wide variety of applications including: diagnosis; prognosis; prediction of disease, stage of disease or disease risk; monitoring disease progression and/or regression; monitoring disease reoccurrence and identifying risk of disease reoccurrence; determining and/or predicting response to treatment and/or treatment outcomes; monitoring and/or predicting treatment compliance or non compliance and the like. The invention further provides a variety of selected molecular markers and a means to identify combinations of the selected molecular markers useful for diagnosing particular traits of interest.

WO 2006/002240 A2

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US05/22071

A. CLASSIFICATION OF SUBJECT MATTER
IPC: C12Q 1/00(2006.01);G01N 33/48(2006.01)
C12Q 1/00(2006.01);G01N 33/48(2006.01)

USPC: 435/4;702/19
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 435/4; 702/19

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 2003/0104499 A1 (PRESSMAN et al.) 05 June 2003 (05.06.2003), page 9, paragraph 0083-0085, page 35, paragraph 0366; page 10 paragraph 0092; page 28, paragraph 0265-0266; pages 35-36, paragraph 0376; page 14, paragraph 0127; page 30, paragraph 0313-0315, 0304, 0307; page 11, paragraph 0098; page 36, paragraph 0397; page 32, paragraph 0329; page 28; paragraph 0262; page 10, paragraph 0094.	1-5, 8-11, 13-20, 22-28, 31, 33-36, 79, 80 --- 6, 7, 12, 21, 29, 30, 32
Y	US 2004/0110221 A1 (TWINE et al.) 10 June 2004 (10.06.2004), page 72, paragraph 0599; page 64; paragraph 0513-0514.	6, 7, 21, 29, 30
Y	US 2003/0073083 A1 (TAMAYO et al.) 17 April 2003 (17.04.2003), page 23, paragraph 0186.	12

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search
16 March 2006 (16.03.2006)

Date of mailing of the international search report
19 APR 2006

Name and mailing address of the ISA/US
Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
Facsimile No. (571) 273-3201

Authorized officer
Jerry Lin

Telephone No. (571) 272 1600

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US05/22071

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of any additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-36,79 and 80

Remark on Protest
- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US05/22071

BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group 1, claim(s) 1-36, 79 and 80, drawn to a method of screening molecular markers by selecting a plurality of markers based on the molecular marker's ability to discriminate.

Group 2, claim(s) 37-77 and 81, drawn to a method of identifying classifiers for a trait by selecting for molecular markers in Tables 1-A-7I.

The inventions listed as Groups 1 and 2 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:
Group 1 has the special technical feature of selecting a plurality of candidate molecular markers based on the molecular marker's ability to discriminate between members of different traits. In contrast, Group 2, has the special technical feature of selecting molecular markers from Tables 1A-7I. Thus the Groups do not share a special technical feature and do not relate to a single general inventive concept under PCT Rule 13.1.

Continuation of B. FIELDS SEARCHED Item 3:
WEST, Medline, Embase, Biosis
Terms: classifier, molecular, marker, population, differential, wald, wolfowitz, mann, whitney, kolmogorov, smirnov, manduchis, database, combination, array, microarray, PCR, differntial, rank, subspace, bagging, boosting